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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,613	02/29/2000	DEBORAH C. MASH	N08-002	8931

7590 01/13/2006

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 01/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/486,613	MASH, DEBORAH C.	
	Examiner	Art Unit	
	Abigail M. Cotton	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-9 and 25-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-9 and 25-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 6-9 and 25-30 are pending in the application as of the response received on December 22, 2005.

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn. Accordingly, claims 6-9 and 25-30 are being examined on the merits herein.

Applicant's arguments, filed December 22, 2005, with respect to the rejection of claims 6-9 and 25-30 under 35 U.S.C. 112, first paragraph, as adding new matter, have been fully considered and are persuasive. In particular, Applicant's amendments to claims 6 and 25 to amend the phrase "alleviate pain treatable with an opioid agonist analgesic" to recite "alleviate pain with an opioid agonist" is believed to present no new matter, as the specification provides support for alleviating pain with an opioid agonist, for example on page 6, first paragraph. Thus, the rejection of claims 6-9 and 25-30 under 35 U.S.C. 112, first paragraph, has been withdrawn.

Applicant's arguments, filed December 22, 2005, with respect to the rejection of claims 25-30 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,925,634 to Olney, have been fully considered and are persuasive. In particular, Olney does not specifically teach "administering" noribogaine to a patient, and instead only teaches

administering its metabolic precursor, ibogaine. It is noted that the administration of ibogaine would necessarily result in the production of the metabolite noribogaine in the body of the patient. However, this administration of ibogaine is not considered to anticipate the administration of noribogaine itself, because the term "administration" is understood by those of ordinary skill in the art as requiring the existence of the compound prior to its administration. *See Schering Copr. V. Geneva Pharmaceuticals, Inc*, 339 F.3d 1373 (Fed. Cir. 2003). Olney does not teach the existence of noribogaine prior to the administration of ibogaine. Thus, the rejection of claims 25-30 under 35 U.S.C. 102(e) over Olney has been withdrawn.

Applicant's arguments, filed December 22, 2005, with respect to the rejection of claims 6-9 under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 5,925,634 to Olney or GB 841,697 (of record) in view of U.S. Patent No. 4,464,378 to Hussain, have been fully considered and are persuasive. In particular, Olney and GB 841,697 do not specifically teach "administering" noribogaine to a patient, and instead only teach administering its metabolic precursor, ibogaine. It is noted that the administration of ibogaine would necessarily result in the production of the metabolite noribogaine in the body of the patient. However, this administration of ibogaine is not considered to anticipate the administration of noribogaine itself, because the term "administration" is understood by those of ordinary skill in the art as requiring the existence of the compound prior to its administration. *See Schering Copr. V. Geneva Pharmaceuticals, Inc*, 339 F.3d 1373 (Fed. Cir. 2003). Olney and GB 841,697 do not teach the existence

of noribogaine prior to the administration of ibogaine, and Hussain does not make up for this deficiency. Thus, the rejection of claims 6-9 under 35 U.S.C. 103(a) over Olney or GB 841,697 in view of Hussain has been withdrawn.

The claims are being newly rejected as follows.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 25-30 are rejected as being unpatentable over U.S. Patent No. 5,591,738 to Howard Lotsof, issued January 7, 1997, in view of Applicant's own admission on pages 3-4 and page 8 of the instant Specification.

Lotsof teaches a method of treating a chemical dependency disorder, an abuse syndrome or combination thereof, by administering an alkaloid (see abstract, in particular.) Lotsof teaches that addiction to drugs such as heroin, methadone, cocaine, amphetamines, caffeine or other substances can be treated (see column 3, lines 40-50,

in particular.) Lotsof also teaches that a suitable alkaloid for treatment is 12-hydroxy ibogaine (noribogaine) (see column 5, line 55 through column 6, lines 55, in particular.)

Lotsof also teaches that a suitable dose of the drug addiction treatment compound may be from about 0.1 mg/kg to about 100 mg/kg (see column 5, lines 43-53, in particular.), and thus teaches an amount that closely overlaps with the "effective amount" as taught by Applicant's and recited for example in claim 27. Furthermore, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of noribogaine administered to a patient, according to the guidance provided by Lotsof, to provide a suitable treatment for drug addiction. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Lotsof does not specifically teach treating pain during the treatment of the chemical dependency disorder, as recited in claim 25.

However, according to Applicant's own admission in the Specification, symptoms associated with drug withdrawal include "nausea, vomiting, anxiety, abdominal cramps, muscle pain, chills and headache" (see paragraph bridging pages 3-4, in particular.) Applicant also admits that the headache and muscular pain are "symptoms commonly

associated [with] this process (see page 8, first full paragraph, in particular.) Thus, according to Applicant's own admission, the patient population of individuals that are in the process of withdrawing from addictive drug use is also a population that commonly experiences headaches and muscular pain, i.e. a population that commonly is subject to pain.

Accordingly, as the patient population that is in the process of withdrawing from addictive drug use overlaps with the patient population that experiences pain, due to headache and/or muscular pain as manifestations of withdrawal symptoms as admitted by Applicant, it is considered that the addictive drug treatment with noribogaine of Lotsof also constitutes a treatment for pain, because Lotsof teaches administration of the noribogaine drug as claimed and according to the method steps as claimed, to a patient population that is subject to pain. Thus, claim 25 is considered to be obvious over the teachings of Lotsof and Applicant's own admission in the instant specification.

It is furthermore noted that since the combined teachings of Lotsof and Applicants own admission renders the administration of the claimed composition obvious, the properties and effect of such a claimed composition will also be rendered obvious by the prior art teachings, since the properties, namely the treatment of pain, are inseparable from its composition. Therefore, if the prior art teaches the composition or renders the composition obvious, then the properties are also taught or rendered obvious by the prior art. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed.

Cir. 1990.) See MPEP 2112.01. The burden is shifted to Applicant to show that the prior art method of using the product does not possess or render obvious the same properties as the instantly claimed method.

It is furthermore noted that, for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, the transitional phrase "consisting essentially of," for example as recited in claim 25, is being construed as equivalent to "comprising," absent a clear indication in the specification or claims of what is meant by, i.e. what is being excluded from the composition by, the phrase "consisting essentially of." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355, and MPEP 2111.03.

Regarding claim 26, Lotsof teaches that noribogaine is suitable as the compound for treatment of drug addiction, as discussed above. Accordingly, it is considered that one of ordinary skill in the art would find it obvious to provide the noribogaine as the sole active ingredient, and thus the sole analgesic, in the pharmaceutical composition. Regarding claims 27-28, Lotsof teaches a dosage range of the compound that closely overlaps with that claimed, as discussed for claim 25 above. Regarding claims 29-30, the dosage amount taught by Lotsof closely overlaps with that claimed, as discussed for claim 25 above. Furthermore, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of noribogaine administered to a patient, according to the guidance provided by Lotsof, to provide a suitable treatment for drug addiction. It is noted that "[W]here the

general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Claims 25-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over the article entitled "Noribogaine Stimulates Naloxone-Sensitive [^{35}S]GTP$_{\gamma}$S Binding" by Pablo et al, published December 20, 1997, in view of Applicant's own admission on pages 3-4 and page 8 of the instant Specification.

Pablo et al. teaches that noribogaine is a metabolite of ibogaine having efficacy as a full μ-opioid agonist that is believed to explain the ability of ibogaine to block the acute signs of opiate withdrawal (see abstract, in particular.) Pablo et al. also teaches that anecdotal observations by addict self-help groups indicate that drug craving and opiate withdrawal symptoms are blocked after a dose of ibogaine. Accordingly, Pablo et al. teaches that noribogaine is believed to be effective in blocking the acute signs of opiate withdrawal.

Pablo et al. does not specifically teach the treatment of pain associated with opiate withdrawal, as recited in claim 25.

However, according to Applicant's own admission in the Specification, symptoms associated with drug withdrawal include "nausea, vomiting, anxiety, abdominal cramps,

muscle pain, chills and headache" (see paragraph bridging pages 3-4, in particular.) Applicant also admits that the headache and muscular pain are "symptoms commonly associated [with] this process (see page 8, first full paragraph, in particular.) Thus, according to Applicant's own admission, the patient population of individuals that are in the process of withdrawing from addictive drug use is also a population that commonly experiences headaches and muscular pain, i.e. a population that commonly is subject to pain.

Accordingly, as the patient population that is in the process of withdrawing from addictive drug use overlaps with the patient population that experiences pain, due to headache and/or muscular pain as manifestations of withdrawal symptoms as admitted by Applicant, it is considered that the addictive drug treatment with noribogaine of Lotsof also constitutes a treatment for pain, because Pablo teaches the desirability of administration of the noribogaine drug as claimed and according to the method steps as claimed, to a patient population that is subject to pain. Thus, claim 25 is considered to be obvious over the teachings of Pablo et al. and Applicant's own admission in the instant specification.

Regarding the "effective amount" of the noribogaine, as recited in claim 25, it is noted that Pablo et al. teaches an amount of noribogaine that binds to opioid receptors (see pages 110-112, in particular), and thus provides guidance as to the amount of noribogaine required for efficacy of the compound. Furthermore, it is considered that

one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of noribogaine administered to the opiate-addicted individual, according to the guidance provided by Pablo et al, to block signs of opiate withdrawal. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

It is furthermore noted that since the combined teachings of Pablo et al. and Applicants own admission renders the administration of the claimed composition obvious, the properties and effect of such a claimed composition will also be rendered obvious by the prior art teachings, since the properties, namely the treatment of pain, are inseparable from its composition. Therefore, if the prior art teaches the composition or renders the composition obvious, then the properties are also taught or rendered obvious by the prior art. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990.) See MPEP 2112.01. The burden is shifted to Applicant to show that the prior art method of using the product does not possess or render obvious the same properties as the instantly claimed method.

It is furthermore noted that, for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, the transitional phrase “consisting essentially of,” for example as recited in claim 25, is being construed as equivalent to “comprising,” absent

a clear indication in the specification or claims of what is meant by, i.e. what is being excluded from the composition by, the phrase "consisting essentially of." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355, and MPEP 2111.03.

Regarding claim 26, Pablo et al. teaches that noribogaine is suitable as the compound for treatment of opiate addiction, as discussed above. Accordingly, it is considered that one of ordinary skill in the art would find it obvious to provide the noribogaine as the sole active ingredient, and thus the sole analgesic, in a pharmaceutical composition. Regarding claims 27-30, Pablo et al. provides guidance as to the efficacy of noribogaine and its binding to opioid receptors, a discussed for claim 25 above. Furthermore, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of noribogaine administered to a patient, according to the guidance provided by Pablo et al, to provide a suitable treatment for opiate addiction. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Claims 25-30 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 6,348,456 to Mash et al, issued February 19, 2002, in view of Applicant's own admission on pages 3-4 and 8 of the instant Specification.

Mash et al. teaches that an essentially pure noribogaine compound (see abstract, in particular), can be administered for the treatment of chemical dependency related to the used of substances such as heroin, cocaine, marijuana, opium, methadone, and others (see column 5, line 64 through column 6, line 8, in particular.) Mash et al. also teaches that the noribogaine can be administered in a dosage of about 0.1 mg to about 100 mg per kg of body weight per day (see column 6, lines 1-7, in particular), which meets the limitation of being an "effective amount" as recited by Applicants and as recited for example in claim 27. Furthermore, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of noribogaine administered to a patient, according to the guidance provided by Mash et al, to provide desired treatment for chemical dependency. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Mash et al. does not specifically teach the treatment of pain with regards to the treatment of chemical dependency, as recited in claim 25.

However, according to Applicant's own admission in the Specification, symptoms associated with drug withdrawal include "nausea, vomiting, anxiety, abdominal cramps, muscle pain, chills and headache" (see paragraph bridging pages 3-4, in particular.)

Applicant also admits that the headache and muscular pain are "symptoms commonly associated [with] this process (see page 8, first full paragraph, in particular.) Thus, according to Applicant's own admission, the patient population of individuals that are in the process of withdrawing from addictive drug use and chemical dependency is also a population that commonly experiences headaches and muscular pain, i.e. a population that commonly is subject to pain.

Accordingly, as the patient population that is in the process of withdrawing from addictive drug use overlaps with the patient population that experiences pain, due to headache and/or muscular pain as manifestations of withdrawal symptoms as admitted by Applicant, it is considered that the chemical dependency treatment with noribogaine of Mash et al. also constitutes a treatment for pain, because Mash et al. teaches administration of the noribogaine drug as claimed and according to the method steps as claimed, to a patient population that is subject to pain. Thus, claim 25 is considered to be obvious over the teachings of Mash et al. and Applicant's own admission in the instant specification.

It is furthermore noted that since the combined teachings of Mash et al. and Applicants own admission renders the administration of the claimed composition obvious, the properties and effect of such a claimed composition will also be rendered obvious by the prior art teachings, since the properties, namely the treatment of pain, are inseparable from its composition. Therefore, if the prior art teaches the composition

or renders the composition obvious, then the properties are also taught or rendered obvious by the prior art. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990.) See MPEP 2112.01. The burden is shifted to Applicant to show that the prior art method of using the product does not possess or render obvious the same properties as the instantly claimed method.

It is furthermore noted that, for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, the transitional phrase "consisting essentially of," for example as recited in claim 25, is being construed as equivalent to "comprising," absent a clear indication in the specification or claims of what is meant by, i.e. what is being excluded from the composition by, the phrase "consisting essentially of." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355, and MPEP 2111.03.

Regarding claim 26, Mash et al. teaches that noribogaine is suitable as the compound for treatment of chemical dependency, as discussed above. Accordingly, it is considered that one of ordinary skill in the art would find it obvious to provide the noribogaine as the sole active ingredient, and thus the sole analgesic, in a pharmaceutical composition. Regarding claims 27-28, Mash et al. teaches a dosage range of the compound that closely overlaps with that claimed, as discussed for claim 25 above. Regarding claims 29-30, the dosage amount taught by Mash et al. closely overlaps with that claimed, as discussed for claim 25 above. Furthermore, it is considered that one of ordinary skill in the art at the time the invention was made would

have found it obvious to vary and/or optimize the amount of noribogaine administered to a patient, according to the guidance provided by Mash et al, to provide a suitable treatment for drug addiction. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Claims 25-30 are rejected under 35 U.S.C. 103(a) as being obvious over the article entitled "Properties of Ibogaine and its Principle Metabolite (12-hydroxyibogamine) at the MK-801 Binding Site of the NMDA Receptor Complex" to Mash et al, 1995 (hereinafter "Mash et al. article") in view of Applicant's own admission on pages 3-4 and 8 of the instant Specification.

The Mash et al. article teaches that ibogaine an its principle metabolite, 12-hydroxy ibogaine (noribogaine), both act as antagonists to the MK-801 binding site of the NMDA receptor (see abstract, in particular.) The Mash et al. article teaches that this activity is believed to contribute to the ability of 12-hydroxyibogamine and ibogamine to interrupt drug-seeking behavior (see abstract, in particular.) The Mash et al. article further teaches that anecdotal reports from addict self help groups suggest that ibogaine is therapeutically useful in the treatment of both physiological and psychological symptoms associated with withdrawal from opiates, stimulants and ethanol (see page 53, first full paragraph in left hand column, in particular.) The Mash et al. article also

teaches the benefits of noribogaine over ibogaine, by teaching that the noribogaine may potentially have fewer neurotoxic properties than the parent drug (see page 55, right hand column, in particular.) Accordingly, the Mash et al. article teaches that noribogaine is believed to be effective in interrupting drug-seeking behavior, such as in drug withdrawal treatment.

The Mash et al. article does not specifically teach the treatment of pain associated with opiate withdrawal, as recited in claim 25.

However, according to Applicant's own admission in the Specification, symptoms associated with drug withdrawal include "nausea, vomiting, anxiety, abdominal cramps, muscle pain, chills and headache" (see paragraph bridging pages 3-4, in particular.) Applicant also admits that the headache and muscular pain are "symptoms commonly associated [with] this process (see page 8, first full paragraph, in particular.) Thus, according to Applicant's own admission, the patient population of individuals that are in the process of withdrawing from addictive drug use is also a population that commonly experiences headaches and muscular pain, i.e. a population that commonly is subject to pain.

Accordingly, as the patient population that is in the process of withdrawing from addictive drug use overlaps with the patient population that experiences pain, due to headache and/or muscular pain as manifestations of withdrawal symptoms as admitted

by Applicant, it is considered that the drug withdrawal treatment with noribogaine as suggested by the Mash et al. article also constitutes a treatment for pain, because the Mash et al. article teaches the desirability of administration of the noribogaine drug as claimed and according to the method steps as claimed, to a patient population that is subject to pain. Thus, claim 25 is considered to be obvious over the teachings of the Mash et al. article and Applicant's own admission in the instant specification.

Regarding the "effective amount" of the noribogaine, as recited in claim 25, it is noted that Mash et al. teaches an amount of noribogaine that binds to NMDA receptors (see pages 54-56, in particular), and thus provides guidance as to the amount of noribogaine required for efficacy of the compound. Furthermore, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of noribogaine administered to the drug-addicted, according to the guidance provided by the Mash et al. article, to interrupt drug-seeking behavior. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

It is furthermore noted that since the combined teachings of the Mash et al. article and Applicants own admission renders the administration of the claimed composition obvious, the properties and effect of such a claimed composition will also

be rendered obvious by the prior art teachings, since the properties, namely the treatment of pain, are inseparable from its composition. Therefore, if the prior art teaches the composition or renders the composition obvious, then the properties are also taught or rendered obvious by the prior art. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990.) See MPEP 2112.01. The burden is shifted to Applicant to show that the prior art method of using the product does not possess or render obvious the same properties as the instantly claimed method.

It is furthermore noted that, for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, the transitional phrase "consisting essentially of," for example as recited in claim 25, is being construed as equivalent to "comprising," absent a clear indication in the specification or claims of what is meant by, i.e. what is being excluded from the composition by, the phrase "consisting essentially of." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355, and MPEP 2111.03.

Regarding claim 26, the Mash et al. article teaches that noribogaine is suitable as the compound for treatment of drug-seeking behavior, as discussed above. Accordingly, it is considered that one of ordinary skill in the art would find it obvious to provide the noribogaine as the sole active ingredient, and thus the sole analgesic, in a pharmaceutical composition. Regarding claims 27-30, the Mash et al. article provides guidance as to the efficacy of noribogaine and its binding to NMDA receptors, as discussed for claim 25 above. Furthermore, it is considered that one of ordinary skill in

the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of noribogaine administered to a patient, according to the guidance provided by the Mash et al. article, to provide a suitable treatment for drug dependence. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Claims 25-30 are rejected under 35 U.S.C. 103(a) over U.S. Patent No. 5,925,634 to John W. Olney, issued July 20, 1999, in view of the article entitled "Properties of Ibogaine and its Principle Metabolite (12-hydroxyibogamine) at the MK-801 Binding Site of the NMDA Receptor Complex" to Mash et al, 1995 (hereinafter "the Mash et al. article.")

Olney et al. teaches that ibogaine can be safely used to treat neuropathic pain by functioning as an NMDA antagonist that is inherently safe and does not cause the neurotoxic side effects caused by other NMDA antagonist drugs (see abstract, in particular.) Olney et al. teaches that ibogaine exhibits antagonist activity comparable to other known NMDA antagonists, such as MK-801 (see column 8, lines 15-35, in particular.) Accordingly, Olney et al. teaches administering the NMDA receptor antagonist ibogaine to treat neuropathic pain.

Olney et al. does not specifically teach administering noribogaine to a patient, i.e., providing the noribogaine to the patient in a form that exists prior to administration to the patient.

The Mash et al. article teaches that 12-hydroxyibogamine (noribogaine) is the principle metabolite of ibogaine, and that both ibogaine and noribogaine are capable of binding the NMDA receptor and exhibiting antagonist activity (see abstract, in particular.) The Mash et al. article also teaches the benefits of noribogaine, by teaching that the noribogaine may potentially have fewer neurotoxic properties that the parent drug (see page 55, right hand column, in particular.)

Accordingly, one of ordinary skill in the art at the time the invention was made would have found it obvious to provide the noribogaine of the Mash et al. article in the neuropathic pain treatment method of Olney et al, because Olney et al. teaches that the neuropathic pain is treated by ibogaine via antagonist activity with the NMDA receptor in a manner that is safe and with reduced neurotoxicity, and the Mash et al. article teaches that noribogaine has similar NMDA antagonist activity as ibogaine, and may have even less neurotoxicity than its parent compound. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to provide the noribogaine of the Mash et al. article in the neuropathic treatment method of Olney et al. with the expectation of providing a compound having efficacy in the mechanism of treatment of neuropathic pain and that may exhibit even reduced neurotoxicity.

Regarding the "effective amount" of the noribogaine, as recited in claim 25, it is noted that the Mash et al. article teaches an amount of noribogaine that binds to NMDA receptors (see pages 54-56, in particular), and thus provides guidance as to the amount of noribogaine required for efficacy of the compound, and Olney teaches an amount of ibogaine that is typically suitable for treatment of neuropathic pain (see column 8, lines 15-30, in particular.) Furthermore, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of noribogaine administered to the patient experiencing neuropathic pain, according to the guidance provided by the Mash et al. article and Olney, to provide treatment of the pain. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

It is furthermore noted that, for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, the transitional phrase "consisting essentially of," for example as recited in claim 25, is being construed as equivalent to "comprising," absent a clear indication in the specification or claims of what is meant by, i.e. what is being excluded from the composition by, the phrase "consisting essentially of." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355, and MPEP 2111.03.

Regarding claim 26, the Mash et al. article and Olney teach that noribogaine is suitable as compound for the treatment of neuropathic pain mediated by NMDA receptor antagonism, as discussed above. Accordingly, it is considered that one of ordinary skill in the art would find it obvious to provide the noribogaine as the sole active ingredient, and thus the sole analgesic, in a pharmaceutical composition. Regarding claims 27-30, the Mash et al. article provides guidance as to the efficacy of noribogaine and its binding to NMDA receptors, and Olney teaches the amount of ibogaine, and NMDA receptor antagonist, desired for the treatment of neuropathic pain, as discussed for claim 25 above. Furthermore, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of noribogaine administered to a patient, according to the guidance provided by the Mash et al. article and Olney, to provide a suitable treatment for neuropathic pain. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Claims 6-9 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 5,591,738 to Howard Lotsof, issued January 7, 1997, in view of Applicant's own admission on pages 3-4 and 8 of the instant Specification, and further in view of U.S. Patent No. 5,760,044 to Sydney Archer, issued June 2, 1998.

The combined teachings of Lotsof and Applicant's own admission in the instant Specification have been discussed above, and teach administering noribogaine to treat drug dependency and the symptoms of drug withdrawal, including pain in the form of headaches or muscular pain. Accordingly, Lotsof and Applicant's own admission in the instant Specification render obvious treat a patient to alleviate pain with an opioid analgesic by administering systemically an amount of noribogaine that is effective to reduce or eliminate pain.

Lotsof and Applicant's own admission in the instant Specification do not specifically teach concomitantly administering an amount of one or more opioid antagonists, as recited in claim 6.

Archer teaches that naltrexone or naloxone (opioid antagonists) can be administered to treat side effects resulting from drug withdrawal such as cocaine, amphetamine and opiate withdrawal (see abstract, column 3, line 58 through column 4, line 35 and column 12, lines 10-60, in particular.)

Accordingly, one of ordinary skill in the art at the time the invention was made would have found it obvious to provide the naltrexone and/or naloxone opioid antagonists of Archer in the drug withdrawal method of Lotsof and Applicant's own admission in the instant Specification, with the expectation of providing a compound capable of providing further treatment of side effects related to the drug withdrawal.

Note it is considered that "[I]t is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980.) Accordingly, claim 6 is obvious over the teachings of the prior art.

Regarding claims 7-8, Archer teaches dosages of naltrexone and naloxone that are suitable for administration to treat drug withdrawal symptoms (see column 12, lines 49-53, in particular), and teaches that factors such as the route of administration, diet, drug combinations and others are considered in determining the amount to be administered. Accordingly, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of naltrexone or naloxone administered to the patient, according to the guidance provided by archer, to provide suitable treatment for drug withdrawal symptoms. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Regarding claim 9, Archer teaches that the means of administration of the naltrexone or naloxone can be through various conventional modes of drug administration, such as intramuscular and subcutaneous administration (see column 11,

lines 35-42 and column 12, lines 23-35, in particular), which are considered to be transdermal administrations (i.e. through the skin.)

Claims 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over the article entitled "Noribogaine Stimulates Naloxone-Sensitive [^{35}S]GTP$_\gamma$S Binding" by Pablo et al, published December 20, 1997, in view of Applicant's own admission on pages 3-4 and 8 of the instant Specification, and further in view of U.S. Patent No. 5,760,044 to Sydney Archer, issued June 2, 1998.

The combined teachings of Pablo et al. and Applicant's own admission in the instant Specification have been discussed above, and teach administering noribogaine to treat drug dependency and the symptoms of drug withdrawal, including pain in the form of headaches or muscular pain. Accordingly, Pablo et al. and Applicant's own admission in the instant Specification render obvious treat a patient to alleviate pain with an opioid analgesic by administering systemically an amount of noribogaine that is effective to reduce or eliminate pain.

Pablo et al. and Applicant's own admission in the instant Specification do not specifically teach concomitantly administering an amount of one or more opioid antagonists, as recited in claim 6.

Archer teaches that naltrexone or naloxone (opioid antagonists) can be administered to treat side effects resulting from drug withdrawal such as cocaine,

amphetamine and opiate withdrawal (see abstract, column 3, line 58 through column 4, line 35 and column 12, lines 10-60, in particular.)

Accordingly, one of ordinary skill in the art at the time the invention was made would have found it obvious to provide the naltrexone and/or naloxone opioid antagonists of Archer in the drug withdrawal method of Pablo et al. and Applicant's own admission in the instant Specification, with the expectation of providing a compound capable of providing further treatment of side effects related to the drug withdrawal. Note it is considered that "[I]t is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980.) Accordingly, claim 6 is obvious over the teachings of the prior art.

Regarding claims 7-8, Archer teaches dosages of naltrexone and naloxone that are suitable for administration to treat drug withdrawal symptoms (see column 12, lines 49-53, in particular), and teaches that factors such as the route of administration, diet, drug combinations and others are considered in determining the amount to be administered. Accordingly, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of naltrexone or naloxone administered to the patient, according to the guidance

provided by archer, to provide suitable treatment for drug withdrawal symptoms. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Regarding claim 9, Archer teaches that the means of administration of the naltrexone or naloxone can be through various conventional modes of drug administration, such as intramuscular and subcutaneous administration (see column 11, lines 35-42 and column 12, lines 23-35, in particular), which are considered to be transdermal administrations (i.e. through the skin.)

Claims 6-9 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 6,348,456 to Mash et al, issued February 19, 2002, in view of Applicant's own admission on pages 3-4 and 8 of the instant Specification, and further in view of U.S. Patent No. 5,760,044 to Sydney Archer, issued June 2, 1998.

The combined teachings of Mash et al. and Applicant's own admission in the instant Specification have been discussed above, and teach administering noribogaine to treat drug dependency and the symptoms of drug withdrawal, including pain in the form of headaches or muscular pain. Accordingly, Mash et al. and Applicant's own admission in the instant Specification render obvious treat a patient to alleviate pain with

an opioid analgesic by administering systemically an amount of noribogaine that is effective to reduce or eliminate pain.

Mash et al. and Applicant's own admission in the instant Specification do not specifically teach concomitantly administering an amount of one or more opioid antagonists, as recited in claim 6.

Archer teaches that naltrexone or naloxone (opioid antagonists) can be administered to treat side effects resulting from drug withdrawal such as cocaine, amphetamine and opiate withdrawal (see abstract, column 3, line 58 through column 4, line 35 and column 12, lines 10-60, in particular.)

Accordingly, one of ordinary skill in the art at the time the invention was made would have found it obvious to provide the naltrexone and/or naloxone opioid antagonists of Archer in the drug withdrawal method of Mash et al. and Applicant's own admission in the instant Specification, with the expectation of providing a compound capable of providing further treatment of side effects related to the drug withdrawal. Note it is considered that "[I]t is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re

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Regarding claims 7-8, Archer teaches dosages of naltrexone and naloxone that are suitable for administration to treat drug withdrawal symptoms (see column 12, lines 49-53, in particular), and teaches that factors such as the route of administration, diet, drug combinations and others are considered in determining the amount to be administered. Accordingly, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of naltrexone or naloxone administered to the patient, according to the guidance provided by archer, to provide suitable treatment for drug withdrawal symptoms. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

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Claims 6-9 are rejected under 35 U.S.C. 103(a) as being obvious over the article entitled "Properties of Ibogaine and its Principle Metabolite (12-hydroxyibogamine) at the MK-801 Binding Site of the NMDA Receptor Complex" to Mash et al, 1995 (hereinafter "the Mash et al. article"), in view of Applicant's own admission on pages 3-4 and 8 of the instant Specification, and further in view of U.S. Patent No. 5,760,044 to Sydney Archer, issued June 2, 1998.

The combined teachings of the Mash et al. article and Applicant's own admission in the instant Specification have been discussed above, and teach administering noribogaine to treat drug dependency and the symptoms of drug withdrawal, including pain in the form of headaches or muscular pain. Accordingly, the Mash et al. article and Applicant's own admission in the instant Specification render obvious treat a patient to alleviate pain with an opioid analgesic by administering systemically an amount of noribogaine that is effective to reduce or eliminate pain.

The Mash et al. article and Applicant's own admission in the instant Specification do not specifically teach concomitantly administering an amount of one or more opioid antagonists, as recited in claim 6.

Archer teaches that naltrexone or naloxone (opioid antagonists) can be administered to treat side effects resulting from drug withdrawal such as cocaine,

amphetamine and opiate withdrawal (see abstract, column 3, line 58 through column 4, line 35 and column 12, lines 10-60, in particular.)

Accordingly, one of ordinary skill in the art at the time the invention was made would have found it obvious to provide the naltrexone and/or naloxone opioid antagonists of Archer in the drug withdrawal method of the Mash et al. article and Applicant's own admission in the instant Specification, with the expectation of providing a compound capable of providing further treatment of side effects related to the drug withdrawal. Note it is considered that "[I]t is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980.) Accordingly, claim 6 is obvious over the teachings of the prior art.

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provided by archer, to provide suitable treatment for drug withdrawal symptoms. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

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Response to Arguments

Applicant's arguments with respect to claims 6-9 and 25-27 have been considered but are moot in view of the new ground(s) of rejection.

The 132 Declaration submitted by the Applicant on December 22, 2005 and signed by Deborah Mash, has been fully considered.

With regards to Applicant's argument in the 132 Declaration that noribogaine is being used as an opioid agonist, and not as an NMDA antagonist as in the neuropathic pain treatment method of Olney, it is noted that the instant claims are drawn to the alleviation of pain in general, and are not specific to the treatment of nociceptive pain or

pain that is not mediated through NMDA receptors. Thus, the claims as written read on the treatment of all kinds of pain, including those mediated through NMDA receptors such as neuropathic pain as taught by Olney.

Furthermore, it is noted that evidence of unexpected results is required to be reasonably commensurate in scope with the claimed invention. See, e.g., In re Kulling, 897 F.2d 1147, 1149, 14 USPQ2d 1056, 1058 (Fed. Cir. 1990); In re Grasselli, 713 F.2d 731, 743, 218 USPQ 769, 777 (Fed. Cir. 1983). Applicant argues the benefits of treating nociceptive pain with noribogaine, which is not commensurate in scope with the claimed method of treating pain in general.

It is furthermore noted that whether ibogaine and/or noribogaine act at the receptors at which opioid agonists act or not, or as an antagonist of the NMDA receptor, is considered to be a mere mechanism of action of the ibogaine and noribogaine. A mechanism of action of a treatment does not by itself carry patentable weight if the prior art teaches the same or nearly the same method steps. Thus, Applicant's recitation of a different mechanism of action of the prior art method of Olney does not, by itself, distinguish the instant claims over the prior art teachings of the same or nearly the same method steps.

Regarding Applicant's arguments that the prior art teachings indicate that ibogaine and/or noribogaine would never be used alone to treat pain having both

nociceptive and neuropathic attributes, and instead would be combined with a drug such as an opioid to treat the nociceptive pain, it is again noted that the claims as written are drawn to a method of treatment of pain in general, and are not restricted to the treatment of pain having a nociceptive component.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abigail M. Cotton whose telephone number is (571) 272-8779. The examiner can normally be reached on 9:30-6:00, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AMC

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